

combination with Doroshow et al.

Freeman studies the treatment of primary tumors with DOX. Freeman is further concerned with the cardiotoxicity of DOX. Hence, Freeman studies NAC or other thiol compounds and the extent to which they might decrease cardiotoxicity. Freeman is concerned with NAC or other biocompounds decreasing cardiotoxicity, while simultaneously also decreasing the efficacy of DOX as an anti-tumor agent (see for example, Freeman, page 173, col. 1, lines 1-6, and line 21 to the end of column). Finally, Freeman deals with primary tumors and offers the observation that NAC increases the life span of the animals treated with DOX. Freeman observes that in mice increased life span was shown when NAC was administered in combination with doses of 1.5 mg/kg of DOX. This positive phenomena was not observed in mice treated with dosages of 2.5 mg/kg of DOX. In sum, the prior art shows that NAC affords the positive effect against primary tumors when administered to mice in combination with DOX dosages of 1.5 mg/kg or less. The prior art teaches that larger doses are ineffective.

One aspect of the presently claimed invention is the treatment of metastasis. The presently claimed invention is not concerned with cardiotoxicity. Further, the presently claimed invention is not concerned with the potential negative effects of NAC on anti-tumor activity of DOX. Further, Applicants' presently claimed invention demonstrates the synergistically increased activity of DOX against metastasis at doses of 1, 2, 5 and 10 mg/kg, due to NAC. Claim 15, as amended recites a range of DOX between 2 and 10 mg/kg, a range the prior art teaches away from.

There is no teaching in either Doroshow or Freeman which would suggest combining any parts thereof effectively to achieve the presently claimed invention. Furthermore, there is no teaching in Doroshow or Freeman which would suggest modifying any parts thereof to produce the presently claimed invention. Therefore, these references are improper basis for rejection under § 103, and Applicants respectfully request that this rejection be

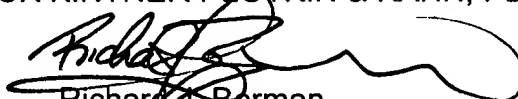
withdrawn and claims 13-15 allowed.

If for any reason, the Examiner feels the application is not now in condition for allowance, it is respectfully requested that the Examiner contact, by telephone, Applicants' undersigned attorney at the indicated telephone number to arrange for an interview to expedite the disposition of this application.

In the event this paper is not timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, along with any other fees which may be required with respect to this application.

Respectfully submitted,

ARENT FOX KINTNER PLOTKIN & KAHN, PLLC

A handwritten signature in black ink, appearing to read "Richard J. Berman", with a large, sweeping flourish extending to the right.

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Enclosures: Marked Up Copy of Claim

RJB:abs



MARKED-UP CLAIM for 09/125,022

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15. (Amended) The method according to claim 13, wherein the doxorubicin is administered in an amount between [1 AND 50]2 and 10 mg per dose.